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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/563,785
Filing Date: April 25, 2006
Appellant(s): NOLTING, JOHN

Anthony Sheldon
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed September 27, 2010 appealing from the Office action mailed April 29, 2010.

(1) Real Party in Interest

The examiner has no comment on the statement identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of the amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of the claimed subject matter contained subject matter is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained I the Appendix to the brief is correct.

(8) Evidence Relied Upon

US Patent or Application Number	Author
2003/0033007	Sirhan et al. (Sirhan et al. B)
2003/0153983	Miller et al.
2004/0002755	Fischell et al.
2004/0249449	Shanley et al.
6,471,980	Sirhan et al. (Sirhan et al. C)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The disclosure as filed does not provide written basis for the new limitation that the plurality of therapeutic agents is released from the plurality of therapeutic coatings after the adjacent overlying timing coating has completely eroded." Specifically the requirement fro complete erosion was not described; therefore this recitation constitutes new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

Claims 12, 14-15 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. in view of Sirhan et al. (henceforth Sirhan et al. reference C).

Miller et al. teach medical devices with a set of layers on their surface that can each contain a different bioactive (see abstract and paragraph 55; instant claim 12). In particular, Miller et al. envision coronary stents as medical devices within their invention (see paragraph 92; instant claim 12). One of ordinary skill in the art at the time of the invention would have found it obvious to select a particular set of therapeutic agents pertinent to the body region treated by the device (e.g. coronary artery). Therapeutic agents considered by Miller et al. are taught to include paclitaxel, dexamethasone, and non-steroidal anti-inflammatory agents (see paragraphs 45 and 49; instant claims 14-15). These therapeutic containing layers are also taught to be composed of biodegradable (bioerodible) polymers (see paragraphs 40-41; instant claim 13). Miller et al. also teach that the layers are applied to any portion of the device, thus it also would have been obvious to apply them to the full length of the device (which includes the distal, proximal, and mid-portions) (see paragraph 50; instant claims 12 and 19-20). The layered configuration contains a plurality of barrier layers (timing coatings) and a plurality of therapeutic agent containing layers that alternate on the surface of the device (see paragraph 62; instant claim 16). These barrier layers are taught to impede the release of therapeutic agents from the device (see paragraph 56; instant claim 18). Embodiments are envisioned where a barrier layer (timing coating) covers each of three therapeutic agent containing layers (see paragraph 62; instant claims 12 and 20). Miller

et al. teach that the layered configuration allows different release profiles of different bioactive agents and can be optimized based upon the desired application (see paragraph 55). The barrier layers (timing coatings) are also taught to be composed of biodegradable polymer and in these instances degradation of the layers controls release of the drug (see paragraphs 32 and 58; instant claims 7 and 12). In view of these teachings, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ bioerodible polymers in the barrier layers and the therapeutic containing layers of Miller et al. Although optimization of the release profile of the contained bioactives is taught, Miller et al. do not explicitly teach sequential release.

Sirhan et al. reference C teaches stents with multiple polymeric coating layers (see column 5 lines 35-62). Classes of drugs also taught present in the coatings of Miller et al. are taught by Sirhan et al. reference C (see column 6 lines 23-29). In addition, Sirhan et al. reference C teaches separate coating layers with individual drugs in each that are released sequentially, as opposed to simultaneously or both sequentially and simultaneously (see example 7; instant claim 1).

Since Sirhan et al. reference C teaches that it was desirable to provide sequential delivery of combinations of drugs with anti-proliferative, anti-thrombin, and immunosuppressive properties from a series of coatings, and Miller et al. teach optimization of the release profiles of similar classes of compounds from their layered coating, it would have been obvious to one of ordinary skill in the art at the time of the invention to configure the layered coating of Miller et al. such that the drugs were

released sequentially (one at a time). Therefore claims 12, 14-15, and 18-20 are obvious over Miller et al. in view of Sirhan et al. reference C

Claims 1-3, 7-12, and 19-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. in view of Sirhan et al. reference C as applied to claims 12, 14-15, and 18-20 above, and further in view of Sirhan et al. (previously cited – see IDS - referred to henceforth as Sirhan et al reference B) and as evidenced by Fischell et al. (previously cited).

Miller et al. Sirhan et al. reference C make obvious a coronary stent with alternating barrier layers (timing coating) and therapeutic agent containing layers that all contain bioerodible polymers and are arranged such that the distal and proximal ends have a plurality of each while the mid-portion has at least one of each. In addition, the claimed therapeutic agents, release kinetics (sequential release) and presence of bioerodible polymers in each layer are also made obvious by Miller et al. in view of Sirhan et al. reference C (see instant claims 1-3, 7-9, and 24-25). Miller et al. in view of Sirhan et al. reference C do not teach that the coronary stent is operably coupled to a catheter or that the therapeutic on the mid-region is different than that on the distal and proximal ends.

Sirhan et al. reference B teaches that an edge effect phenomenon is known to occur in patients that have had coronary stents deployed within them (see paragraph 19). Beyond the edges of the implanted stent severe stenosis often develops, thus the inventors developed a device that focuses drug delivery from the proximal and distal

ends of a stent device that extends beyond the ends of the stent (see paragraph 22). The intermediate portion (mid-portion) of the stent between the distal and proximal regions is taught to have a therapeutic agent that is different and released with a different kinetic profile than that released from the ends (see paragraph 51; instant claims 10 and 21). These therapeutic agents are taught to be present in coating form on the stent (see paragraph 59). Particular therapeutic agents envisioned on the device, separately or in combination, include dexamethasone, rapamycin, rapamycin analogs, and prednisone (see paragraph 35; instant claims 3 and 15). Sirhan et al. reference B teaches that the stent is deployed via a balloon catheter (requiring that the stent and catheter be operably coupled) (see paragraph 48; instant claim 1). In addition, the presence of a biodegradable (bioerodible) rate controlling element (layer) that impedes the delivery of drug from the intermediate region (mid-portion) as compared to the ends to different degrees is also taught (see paragraphs 25 and 33; instant claim 9). Sirhan et al. reference B also teaches that the therapeutic has a higher diffusion rate from the device at the ends than in the intermediate region (mid-portion) (see claim 7; instant claims 11 and 22). Sirhan et al. reference B does not explicitly teach a multi-layered configuration of drug containing coatings.

Since Sirhan et al. reference B and Miller et al. in view of Sirhan et al. reference C both teach drug eluting stents, it would have been obvious to one of ordinary skill to operably couple the stent of Miller et al. in view of Sirhan et al. reference C to a catheter so as to facilitate implantation. In addition, it also would have been obvious to configure the coating of Miller et al. in view of Sirhan et al. reference C in consideration of the

stent edge effects as taught by Sirhan et al. reference B. This would yield a stent where the distal and proximal ends have at least two different drug coatings and two barrier (timing) coatings that alternate and can also have the intermediate (mid-region) portion with drug (different from that on the distal and proximal ends) coating and a barrier coating. This triumvirate of drugs would be obvious considering that Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B teach a collection of drugs all known for the same purpose (treating restenosis) and their combination in and subsequent liberation from a stent would have been obvious (see "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) see MPEP 2144.06 and instant claims 8, 10, 26, and 28-29.) From the teachings of Sirhan et al. reference B, the claimed differences in diffusion characteristics between the distal/proximal regions and intermediate region would follow from the combination of references. Further, since Miller et al. in view of Sirhan et al. reference C teach sequential delivery of drugs from their taught layered configuration, sequential delivery of the multiple drugs from the separate layers on the distal and proximal ends would also have been obvious.

Sirhan et al. reference B provides for the deployment of the stent made obvious by their teachings and those of Miller et al. in view of Sirhan et al. reference C to a vessel. Fischell et al. teach a coated stent where a biodegradable polymer containing

barrier layer is on top of a drug layer to control its rate of release (see paragraph 49). They go on to teach that the thickness of the biodegradable is determined by its erosion properties (see paragraph 54). This indicates that the rate of erosion of a biodegradable barrier layer is directly related to the rate of release of the drug from its layer and that such polymer layers are actuated by erosion (see instant claims 1, 23, and 27). Since the polymers in each of the layers are taught to be biodegradable, they would be capable of controlling delivery of drug via erosion. So it then follows that the deployment of the device made obvious by Miller et al. in view of Sirhan et al. reference C and Sirhan et al. B that is configured to sequentially deliver the drugs from the distal and proximal ends would do so via the sequential actuation/erosion of overlying layers (e.g. erosion of top barrier allows delivery of first therapeutic; erosion of polymer in first therapeutic layer allows erosion of second barrier layer which then allows delivery of second therapeutic). Furthermore, instant claim 23 contains several active steps that are physiological processes that occur due to the implantation of the claimed stent. No action by man is required or needed after deployment of the device to release the drug, erode the polymer of the first therapeutic coating, or actuate the first timing coating to release the second therapeutic. Fischell et al. demonstrate that the delivery mechanism claimed by the instant claims (e.g. instant claims 1 and 23) was known to occur in the claimed degradable barrier layer-drug layer configuration, which was made obvious by Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B; thus the device of this modified reference would have necessarily functioned in this way upon implantation. Appellant has provided no teachings delineating a subpopulation of

particular bioerodible polymers that are necessary to perform in the claimed capacity; therefore, it is the position of the examiner that even in the absence of the teachings of Fischell et al., the release of drug from the stent made obvious by Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B would occur via the claimed method upon deployment to a vessel *in vivo*. Thus claims 1-3, 7-12, and 19-29 are obvious over Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B and as evidenced by Fischell et al.

Claims 12 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. in view of Sirhan et al. reference C as applied to claims 12, 14-15, and 18-20 above, and further in view of Shanley et al. (US PGPub No. 2004/0249449).

Miller et al. in view of Sirhan et al. reference C make obvious a coronary stent with alternating barrier layers (timing coating) and therapeutic agent containing layers that all contain bioerodible polymers and are arranged such that the distal and proximal ends have a plurality of each while the mid-portion has at least one of each. In addition, the claimed therapeutic agents, release kinetics (sequential release) and presence of bioerodible polymers in each layer are also made obvious by Miller et al. in view of Sirhan et al. reference C (see instant claim 12). Miller et al. in view of Sirhan et al. reference C do not explicitly teach that the therapeutic agents are released from their respective layers after the adjacent overlying timing coating has completely eroded.

Shanley et al. teach a medical device intended for delivery of therapeutic agents to blood vessels (see paragraph 41). In this device are regions that contain layers of

different therapeutic agents such that different agents are released at different times (see paragraph 94). In a particular, Shanley et al. teach that the different layers are eroded sequentially so that the majority of a therapeutic in a first layer is released before the majority of a therapeutic agent in an underlying layer (see paragraph 94).

Since Shanley et al. teach sequential delivery of therapeutic agents from separate erodible layers via the sequential erosion of each layer, it would have been obvious to one of ordinary skill in the art to utilize such a phenomenon in the invention of Miller et al. in view of Sirhan et al. reference C since they also provide sequential release of therapeutic agents from separate bioerodible layers. Given that Miller et al. in view of Sirhan et al. reference C also teaches that their bioerodible barrier layers control the rate of release of therapeutic agents, the teachings of Shanley et al. would translate to the overlying barrier layer for a given therapeutic agent containing layer eroding before the therapeutic agent containing layer beneath it. Consequently, the barrier layer would completely erode before its underlying therapeutic containing layer. In addition, it would then follow that in some embodiments encountered via routine experimentation some amount of therapeutic agent would remain in this underlying layer after the erosion of barrier layer and would be released by the time the therapeutic containing layer completely eroded. Therefore claims 12 and 31 are obvious over Miller et al. in view of Sirhan et al. reference C and Shanley et al.

Claims 1, 23, 30, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. in view of Sirhan et al. reference C and Sirhan et al.

reference B and as evidenced by Fischell et al. as applied to claims 1-3, 7-12, and 19-29 above, and further in view of Shanley et al.

Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B and as evidenced by Fischell et al. make obvious the products and methods as recited in claims 1 and 23 where the layered coating configuration provides sequential delivery of different therapeutic compounds one at a time. This modified reference does not explicitly teach that the therapeutic agents are released from their respective layers after the adjacent overlying timing coating has completely eroded.

Shanley et al. teach a medical device intended for delivery of therapeutic agents to blood vessels (see paragraph 41). In this device are regions that contain layers of different therapeutic agents such that different agents are released at different times (see paragraph 94). In a particular, Shanley et al. teach that the different layers are eroded sequentially so that the majority of a therapeutic in a first layer is released before the majority of a therapeutic agent in an underlying layer (see paragraph 94).

Since Shanley et al. teach sequential delivery of therapeutic agents from separate erodible layers via the sequential erosion of each layer, it would have been obvious to one of ordinary skill in the art to utilize such a phenomenon in the invention of Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B as evidenced by Fischell et al. since they also provide sequential release of therapeutic agents from separate bioerodible layers. Given that Miller et al. in view of Sirhan et al. reference C and Sirhan et al. reference B as evidenced by Fischell et al. also teaches that their bioerodible barrier layers control the rate of release of therapeutic agents, the

teachings of Shanley et al. would translate to the overlying barrier layer for a given therapeutic agent containing layer eroding before the therapeutic agent containing layer beneath it. Consequently, the barrier layer would completely erode before its underlying therapeutic containing layer. In addition, it would then follow that in some embodiments encountered via routine experimentation some amount of therapeutic agent would remain in this underlying layer after the erosion of barrier layer and would be released by the time the therapeutic containing layer completely eroded. Therefore claims 1, 23, 30, and 32 are obvious over Miller et al. in view of Sirhan et al. reference C, Sirhan et al. reference B ., and Shanley et al. and as evidenced by Fischell et al.

(10) Response to Argument

Rejection of claims 30-32 under 35 USC 112, first paragraph:

Appellant argues that figure 3 and paragraphs 38 and 40 provide written basis for the recitation that the therapeutic in a given coating is released "after the adjacent overlying timing coating has completely eroded." This argument is not persuasive. Figure 3 is described as depicting the release of therapeutic from the coated stent. While the arrow symbols in this figure clearly translate to the passage of time corresponding to the timing coatings, it is not clear that they represent the complete or partial erosion of these layers. There is no discussion of the phenomenon in the stent that is represented by these arrows provided by the specification. Although paragraphs 38 and 40 discuss the erosion of the timing coatings occurring before the release of the

therapeutic agent for the adjacent underlying coating, there is no statement or suggestion that the timing coating must be completely gone before the release of the therapeutic commences. Therefore the recitation released "after the adjacent overlying timing coating has completely eroded" in claims 30-32 is new matter and does not have written basis in the original disclosure.

Rejection of claims 12, 14, 15, and 18-20 under 35 USC 103(a) over Miller et al. in view of Sirhan et al. C:

Appellant summarizes some of the teachings found in Miller et al. and Sirhan et al. C; however these embodiments are a subset of those taught and suggested by these references. While Miller et al. do teach control of the rate of release of bioactive by the diffusion of bioactive agent from a polymer matrix through a less permeable overlying bioactive free barrier layer, Miller et al. also teach that these annular layers are biodegradable (and therefore erodible), indicating the presence of additional release mechanisms in the layered system. The biodegradable polymers envisioned by Miller et al. are also well known to be bioerodible. Such materials in the barrier layer would erode over time, as occurs in the instant layers, thereby providing the same mechanism of delivery touted by appellants. Thus their use as the barrier layers taught by Miller et al. results in a device with the same materials and delivery mechanism instantly claimed. Further, Miller et al. also teach the selection of different compositions for the layers to optimize the release profile of the contained drugs for the artisan's desired use which indicates that embodiments in addition to those explicitly described were envisioned by

Miller et al. Therefore the controlling phenomena for the release of bioactive agents from the layered coating configuration is not limited to diffusion, as suggested by appellants, and Miller et al. explicitly direct the artisan of ordinary skill to modify their teachings by selecting components for the layers to achieve the artisan's desired profile of release.

In their summary of a subset of the teachings of Sirhan et al. C, appellant suggests that this reference only provides for release of the active agents contained in their layered coating by diffusion. This is not the case because Sirhan et al. C also teaches degradable/bioerodible rate controlling layers over the drug reservoir, indicating an additional release mechanism. Moreover, the teachings of Sirhan et al. C are not limited to any one of the multiple embodiments that they discuss. Appellant further argues that this reference does not provide teachings of exclusive and sequential release of a plurality of therapeutic agents from a plurality of therapeutic coatings without the release of therapeutic agents from the other therapeutic coatings. Sirhan et al. C explicitly teach a series of coating layers with different therapeutic agents in each from which the drugs are released simultaneously and/or sequentially (see example 7). These temporal releases cover all of the possible options for the release of multiple therapeutics from a coating. A time block can have one of these temporal releases or both. "Sequential" means the successive order of two or more things and "exclusively" was interpreted as indicating that only one therapeutic at a time was released, which does not change the definition of sequential; therefore the teachings of sequential delivery by Sirhan et al. C meets the limitation of "exclusively and sequentially without

the release of the therapeutic agents from other of the therapeutic coatings." Since simultaneous delivery, sequential delivery, or simultaneous and sequential delivery are the only three options available for delivery of multiple therapeutics from a coating, it would have been obvious for the artisan of ordinary skill in the art to select any one of them. Consequently, when the teachings of temporal controlled release of therapeutic agents from the layered coating of Sirhan et al. C are combined with those of Miller et al., the sequential delivery of the therapeutics contained in the layered coating configuration as instantly claimed would have been obvious to the artisan of ordinary skill. These references would have been obvious to combine because both teach 1) a layered coating configuration on a stent where a layer of drug with polymer is overlaid with a polymer only layer to control the release of drug, 2) a series of layers of polymers with different drug in each drug layer, 3) biodegradable polymers that are also bioerodible for the polymeric rate controlling layers, and 4) Miller et al. suggest optimization of drug release from their layered configuration while Sirhan et al. C teaches different desired release profiles. Miller et al. teach timing coatings as their barrier layers which alternate with therapeutic coatings that they describe as drug containing matrix polymer layers on the full length of a stent, while Sirhan et al. C teaches sequential drug delivery from such a configuration is desirable. The full length of a stent includes the proximal, distal, and middle regions instantly claimed. Therefore the combination of these references renders the instant invention obvious.

Rejection of claims 1-3, 7-12, and 19-29 under 35 USC 103(a) over Miller et al. in view of Sirhan et al. C, Sirhan et al. B, and Fischell et al.:

Appellant reiterates their arguments presented against the rejection made over Miller et al. in view of Sirhan et al. C. which were addressed above. These remarks are similarly reiterated.

Rejection of claims 12 and 31 under 35 USC 103(a) over Miller et al. in view of Sirhan et al. C and Shanley et al.:

Appellant reiterates their arguments presented against the rejection made over Miller et al. in view of Sirhan et al. C. which were addressed above. These remarks are similarly reiterated.

Rejection of claims 1, 23, 30, and 32 under 35 USC 103(a) over Miller et al. in view of Sirhan et al. C, Sirhan et al. B, Fishcell et al., and Shanley et al.:

Appellant reiterates their arguments presented against the rejection made over Miller et al. in view of Sirhan et al. C. which were addressed above. These remarks are similarly reiterated.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Caralynne Helm/
Examiner, Art Unit 1615

Conferees:

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615

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